

Development of Options to Encourage Animal Drug Approvals for MINOR SPECIES and MINOR USES

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COMMENTS

H. Dennis McCurdy, D.V.M.
Mid-America Veterinary Research Consulting
9910 Ballentine Street
Overland Park, KS 66214-2342
Phone (913) 888-0384
FAX (913) 888-4866

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Personal Background:

I have spent 23 years in developing pharmaceutical products primarily for small animals. During that time, I had direct responsibility for 19 new or supplemental label approvals. Since becoming employed by industry, I have responded to all requests for input, concerning the development of regulations and guidelines that were in my area of product development.

During my industry years, I repeatedly experienced the demand for minor uses and minor species. Each time a new product I was responsible for reached the market, I would be deluged with requests. The requests were for everything from basic data to product for "experimental uses". This effort was not a part of my job description as "there was too much work involved with little or no benefit to the company."

General:

The overall purpose of this regulatory effort should be to assist the practitioner in dealing with drug availability concerns. The drug approval process is intended to provide adequate data to aid with appropriate drug selection. The *Minor Use/ Minor Species* initiative presents some unique challenges to the Center for Veterinary Medicine (CVM) in the attempt to provide approved drugs where none now exist. This is a commendable effort to assist in reducing the drug availability concerns that face the veterinary profession.

Where will the products for minor uses and minor species come from? Personal experience suggests that the majority of products for use in exotic and zoo

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animals, as well as many for other species of animals, will come from drugs already available to practitioners. The demand will stem from the practitioner's desire for the use of safe, effective therapeutic regimens. New chemical entities will play a relatively minor role, at least until industry identifies the potential size of markets that have yet to be addressed. The basic costs of pharmaceutical development, regardless of regulatory demands, will still limit the development of new chemical entities for minor uses and minor species, unless significant incentives or outside funding is available. The proposed regulations need to adequately address new minor use and/ or minor species labels for existing approved products.

Minor Species:

In an effort to reduce drug availability concerns, one objective should be to promote the development of adequate data for minor species uses of approved products. New drugs always stimulate a flurry of off label uses as soon as these products reach the market. Effort needs to be placed on the development of quality data when the drug is provided for "experimental uses". If there was a reasonable opportunity for industry to gain claims for such uses at a reasonable cost, they may be encouraged to collect and submit the data.

Academicians and researchers are constantly looking to find alternative products to meet practitioner needs. The major challenge with the current approach is that often only partial data on safety and efficacy are being generated. More quality research would be stimulated if industry had an increased incentive to participate more vigorously than they do at this time.

Minor species practitioners have no choice but to experiment on animals belonging to their clients. If they are lucky, the experiment works, but what if it does not work. Successes are passed on to other practitioners who also must experiment on perhaps a different breed of that species. This is the current situation for exotic and zoo practitioners. It is a steadily growing area of veterinary practice that is essentially being ignored by industry and the CVM. While the numbers of these animals are few, their value is often great, particularly in terms of replacement.

Some minor species of animals are considered food animals, *e.g.*, food fish, sheep and goats. Such species must be dealt with separately to protect public health.

The collection of safety data for exotic species will be a significant challenge. An acceptable alternative must be developed to the requirements for target species safety testing. One approach is to discuss the need for safety data with experts in that area of veterinary medicine. Minimum requirements for safety data, as well as possible alternatives, could be developed from such discussions.

Recommendations for Minor Species:

1. Facilitate the process for “experimental product uses”. Allow distribution of marketed products for such uses so long as the investigator provides minimal safety and efficacy data on those applications.
2. One of the most expensive and most limiting requirements for approval is the clinical field trial. Rather than the current field trial requirement, develop a system of initial “provisional approval” and monitor the product uses, specifically safety and efficacy, until sufficient field data are collected to support one or more claims.

Minor Uses:

There are several different minor use areas to consider. Perhaps the area of greatest value to the industry is new product labels for a limited market where no products currently exist. One small animal example is a systemic medication to treat systemic fungal infections. Such a product is expected to have limited geographic distribution. The current cost of development of a systemic antifungal product, in spite of the presence of human products, will not allow the consideration of such a product for veterinary use.

Currently, practitioners are using approved human products where veterinary products do not exist. Allowing the submission of clinical data in support of a veterinary application would promote the safe, effective use of such products. Significant numbers of actual clinical cases could provide all the data necessary to evaluate product performance for establishing a veterinary claim. Such uses would generate negligible environmental impact, based on their minor use designation. As these drugs are approved human products, they have already met acceptable manufacturing requirements. Non-food animal uses would not involve food safety concerns. Food animal applications would require minimal residue and method development to protect the public, based on the level of use and risk to the public, as well as the chemical category of the product.

Another minor use area is the use of an existing veterinary product off label. The submission of clinical data, as discussed above, would again support a label claim.

The most difficult area to address is the need for a minor use new drug application. The incidence of conditions requiring such a drug would impact any decision to develop the product. Incidence data could also be used to assist the CVM in determining the approval requirements for such a product. If the uses are minor enough, for example, sufficient performance data may be gained from

actual clinical use collected under experimental use conditions. If expanded uses of such a product occurred, additional data may be required to support those uses.

Recommendation for Minor Uses:

- Allow the use of practitioner-generated clinical field data in support of product approval for minor uses and minor species claims.

SPECIFIC REQUESTS FOR COMMENTS:

A. Scope:

- In part, the designation of minor use and minor species can be defined based on the market for such products. The current definition for minor species appears adequate at this time. Similarly, minor uses could be defined as necessary product uses for which the current approval process is unreasonably restricting product development.

B. Creating Additional Statutory Authority:

- Safety and effectiveness data for minor uses and minor species should be impacted by all data that are available. The collection of basic laboratory data could be waived in the presence of significant clinical use information demonstrating product performance under actual use conditions. Such data provide more meaningful data to practitioners than basic laboratory evaluations.
- The standards for drug approval for minor species and minor uses should be different from major species, based on the classification of the animal species being dosed. The requirements for minor uses and minor species should be adjusted, based on the risk associated with that use.
- The labeling should reflect the data collected to prepare the label, as it does with existing labels. For example, the label for a minor species or minor use should indicate the animal species involved in the claim, as well as the performance data (safety and efficacy) to establish the claim. If there is a requirement to indicate the FDA approval on other animal drugs, then the difference in approval could be indicated, if necessary, through the use of unique approval numbers.
- Dosages of minor use or minor species products, in most cases, would be based on current field use data. Sufficient data may be available in practitioner medical records to support safe, effective product use.

application could be found to be approvable. Should the foreign requirements for the approval that was granted meet or exceed FDA requirements, then consideration for the minor use or minor species label could be considered based on the foreign approval.

- The potential for product review outside the CVM could be a consideration if appropriate contractual arrangements were established, subject to appropriate monitoring by the FDA. Compensation for such a review must be through appropriate funding to avoid any question of impropriety.
- Expert panels or compendia should be considered as it applies to pending minor use or minor species product claims, so long as the opinions or data support a prevailing professional position. Such opinions or data should provide reasonable facts to assure that the claimed uses will be safe and effective when used according to the proposed labeling. If a monograph were available to support such a product use, it could be considered as it supported the application.

C. Administrative and Regulatory Changes:

- The existing manufacturing standards produces quality products similar to human medicine. Manufacturing standards for minor use and minor species products should be based on requirements similar to those previously used for veterinary products. Those standards have a history of providing adequate quality for the veterinary profession. Because of the history behind these standards, no label comments are necessary.

D. Creating Incentives:

- Successful incentives are those that would provide the product sponsor with an acceptable return on the investment in the final product. Which incentives will depend on the corporate structure. Selection, therefore, could be through a confidential process of negotiation with the sponsor, designed to be fair to all participants in the program.
- Alternative financial support should be acceptable to industry and the CVM so long as it does not interfere with the collection of appropriate data or the preparation of a product with adequate quality.
- A viable alternative to the new animal drug approval process is the creation of a national medical record database, collecting all the important facts from complaint through post-treatment assessment. When shared with the profession, such a database will provide veterinary practitioners with the facts needed to select an appropriate minor species or minor use product under AMDUCA, thereby reducing drug availability concerns.

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